comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group II. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A7, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group III. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A8, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group IV. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A9, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group V. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-AG and S100-A7, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group VI. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-AG and S100-A8, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group VII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-AG and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group VIII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A7 and S100-A8, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group IX. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A7 and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group X. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A8 and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XI. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-AG, S100-A7, and S100-A8, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-AG, S100-A7 and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XIII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-A7, S100-A8, and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XIV. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for diagnosis, wherein said method comprises detecting S100-AG, S100-A7, S100-A8, and S100-A9, and a kit comprising a component for detecting proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XV. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XVI. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A7, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XVII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A8, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XVIII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A9, and a kit comprising a component for detecting said protein, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XIX. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG and S100-A7, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XX. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG and S100-A8, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXI. Claims 1-7, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A7 and S100-A8, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXIII. Claims 1-7 and 14-18, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A7 and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXIV. Claims 1-7, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A8 and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXV. Claims 1-7, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG, S100-A7, and S100-A8, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXVI. Claims 1-7, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG, S100-A7 and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXVII. Claims 1-7, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-A7, S100-A8, and S100-A0, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXVIII. Claims 1-7, insofar as the claims are drawn to a method for prognosis, wherein said method comprises detecting S100-AG, S100-A7, S100-A8, and S100-A9, and a kit comprising a component for detecting said proteins, classified in class 435, subclass 7.1 and, for example, in class 530, subclass 388.1.

Group XXIX. Claims 8-13, drawn to a method for diagnosis, wherein said method comprises detecting autoantibodies, and a kit comprising a component for detecting said autoantibodies, classified in class 436, subclass 7.1 and, for example, in class 530, subclass 350.

Group XXX. Claims 24-32, drawn to a method for immunizing a host, wherein said method comprises inoculating said host with S100-AG, classified in class 424, subclass 184.1.

Group XXXI. Claims 24-32, drawn to a method for immunizing a host, wherein said method comprises inoculating said host with S100-A7, classified in class 424, subclass 184.1.

Group XXXII. Claims 24-32, drawn to a method for immunizing a host, wherein said method comprises inoculating said host with S100-A8, classified in class 424, subclass 184.1.

Group XXXIII. Claims 24-32, drawn to a method for immunizing a host, wherein said method comprises inoculating said host with S100-A9, classified in class 424, subclass 184.1.

In support of the present restriction requirement, the Examiner has alleged that the subject matter of the pending claims represents thirty-three distinct inventions. The Examiner maintains that the inventions in groups I-XXIX as disclosed are biologically and chemically distinct, unrelated in structure and/or function, and/or made by and/or used in different methods, and therefore, are distinct inventions. The Examiner further alleges that the inventions in groups I-XXXIII as disclosed are materially different methods that differ in objectives, method steps, reagents and/or doses and/or schedules used, response variables, assays for end products and/or results, and criteria for success and, therefore, the claimed methods are distinct.

For reasons set forth below Applicants respectfully traverse the requirement for restriction and request that the pending claims of the application be grouped into the following three groups:

Claims 1-7 and 14-8 directed to methods and kits for detection of S100 proteins as diagnostic and prognostic markers of cancer;

Claims 8-18 directed to directed to methods and kits for detection of S100 autoantibodies as diagnostic and prognostic markers of cancer; and

Claims 24-32 directed to methods of immunizing a patient with S100 proteins.

As set forth in MPEP §103, the following two criteria must be satisifed for a proper requirement for restriction between patentable distinct inventions:

(i) the inventions must be independent or distinct as claimed; and

(ii) there must be a serious burden on the examiner if restriction is required.

In addition, with regard to claims containing Markush-Type groups, such as the claims pending in the present case, "if the members of the Markush group are sufficiently few in number or so clearly related that a search and examination of the entire claim can be made without a serious burden, the examiner must examine all members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions.

The present invention provides methods, reagents, and kits for detection of S100 proteins, or S100 autoantibodies, as markers of cancer. As set forth in the specification, S100 proteins are low molecular weight proteins *related to one* another by their (i) ability to bind calcium and (ii) possession of EF-hand domains. Because the S100 proteins are related proteins, autoantibodies specific for such proteins would also be expected to share physical properties.

Applicants assert that given the structural similarities between the different S100 proteins and different S100 autoantibodies, the claims do not represent a class of molecules "unrelated in structure and/or function." It should also be noted that a result from the method of claim 1 or 8 which shows an elevation of only one specified S100 protein or S100 autoantibody may indicate one type of cancer, while a test result showing elevation of a different S100 protein or autoantibody, or mixture of S100 proteins or autoantibodies, may be indicative of a second type of cancer. ***In either case, the steps of the method and objective of the method, i.e, determining the presence of cancer, are identical.***

Additionally, in the present instance, claims 1-7 are directed to methods for the diagnosis and prognosis of cancer in a subject wherein said methods involve detection of at least one S100 protein. Claims 8-13 are directed to a methods for the diagnosis and prognosis of

cancer in a subject wherein said methods involve detection of autoantibodies specific for at least one S100 protein. Independent claims 1 and 8 refer to only ***four*** Markush-Type groups "*selected from the group consisting of S100-AG, S100-A7, S100-A8 and S100-A9. selected from the group consisting of S100-AG, S100-A7, S100-A8 and S100-A9.*

Applicants assert that even if, for argument's sake, the specified S100 proteins were independent and distinct inventive entities, the members of the Markush group are sufficiently few in number, *i.e.*, four, and so clearly related by structure, that a search and examination of the entire claim could be made without a serious burden (see MPEP §103).

The Examiner has further restricted the claims into different groups based on whether the claims are directed to methods of diagnosing cancer versus methods for prognosing cancer. Applicants assert that such a restriction is clearly erroneous, because the steps of the claimed methods are virtually identical regardless of whether one is diagnosing cancer or prognosing cancer. In each instance, the claims encompass methods for detection of S100 protein or S100 autoantibody levels. The only distinction between methods for diagnosing cancer versus prognosing cancer is that for a diagnostic test there will normally be a single determination of S100 protein or autoantibody levels, while for a prognostic test determination of S100 protein or autoantibody levels, are detected for sequential samples from a single subject.

For reasons set forth above, Applicants respectfully traverse the Examiner's restriction requirement. However, in order to be fully responsive to the requirement for restriction, Applicants elect, with traverse, the subject matter of Group XIV claims.

The Examiner has also indicated that claims 1, 8 and 24-26 are generic to a plurality of disclosed patentably distinct species wherein said cancer is selected from the group consisting of (i) lung cancer (ii) breast cancer and (iii) colon cancer. The Examiner request that Applicants elect a single disclosed species. Applicants elect, with traverse, the species of lung cancer.

Withdrawal of the requirement for restriction and favorable consideration and allowance is earnestly solicited.

Respectfully submitted,

Rochelle K. Seide
PTO Reg. No. 32,300

Carmella L. Stephens
PTO Registration No. 41,328
ATTORNEYS FOR APPLICANTS

(212) 408-2539

BAKER BOTTS, L.L.P
30 Rockefeller Plaza
New York NY 10112